

P044 Tumour cell-bone marrow stromal cell interactions modify expression of Cathepsin K, ADAMTS-15, TIMP-3 and osteoprotegerin (OPG)

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Introduction: Proteases and their inhibitors are implicated in mediating tumour spread to distant sites (including bone), and may be produced both by tumour cells and the surrounding non-malignant cells. Enzyme expression and activity is regulated by complex cell-cell and cell-matrix interactions, as well as the balance between enzymes and their endogenous inhibitors. We have investigated whether interactions between breast cancer and bone marrow stromal cells (BMSCs) affect gene expression of proteases and TIMP3. Methods: MDA-MB-436 breast cancer cells transfected with GFP (MDA-G8) and human BMSCs were grown individually or as co-cultures for 72h, and cells from the mixed population were subsequently separated using flow cytometry. Alternatively, MDA-G8 cells were cultured for 72h in BMSC conditioned medium. Changes in expression of cathepsin K, ADAMTS-8, ADAMTS-15 and TIMP3 in the individual populations were assessed by real-time RT-PCR. Expression of the bone-related protein OPG was also analysed. Results: Following co-culture we detected a decrease in cathepsin K, TIMP3, ADAMTS-15 and OPG expression by BMSC, and a corresponding increase in tumour cell expression, compared to the levels detected when cells were cultured separately. No significant change in gene expression was detected in tumour cells grown in BMSC conditioned medium. Conclusions: Our data demonstrate that expression of genes potentially involved in tumour spread to bone, is modulated by direct contact between tumour cells and the cells of the bone microenvironment.